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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,872	10/22/2003	Jane Hirsh	CP 107P	6830

23579 7590 08/31/2006

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,872	HIRSH ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/2/06, 9/30/05...
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application claims priority to multiple provisional applications. It is noted that the concept of the "pulsatile release" formulation of milnacipran was introduced in the 60/431,861 application, and as such the priority date for this terminology was considered by the examiner to be 12/09/2002.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1 – 9 and 11 – 24 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 – 4 and 10 – 28 of copending Application No. 11/192,697. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 – 3, 6 – 18, and 20 – 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 3, 6 – 18, and 20 – 24 of copending Application No. 10/691,936. Although the conflicting claims are not identical, they are not patentably distinct from each other because the delayed or extended release milnacipran formulation of claim 1 is within the scope of the instant claims, as extended release dosage forms are defined in the '936 application as those that "allow at least a twofold reduction in dosing frequency as compared to that drug presented as a conventional form," which is within the scope the definition of a pulsatile release dosage form on page 16 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 14 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 3, 9, 12, and 14 – 17 of U.S. Patent

No. 7,038,085. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are directed to formulations and methods of using para-hydroxy-milnacipran as a treatment for depression, especially in light of the specification which states that the formulation may comprise an immediate release portion of a formulation in combination with an extended release portion (column 24, lines 28 – 33), and therefore meets the limitations of a pulsed release formulation of para-hydroxy-milnacipran.

Specification

The disclosure is objected to because of the following informalities: the limitation of claim 14 wherein the milnacipran is in the form of a therapeutically equivalent does of para-hydroxy-milnacipran (F2782) is not specifically recited in the specification. The limitation of claim 18 that the formulation may comprise from 100 to 600 mg of modafinil is not disclosed in the specification. Additionally, the limitation of claim 22 that the kit should comprise instruction on taking the formulation once daily before bedtime is not specifically recited. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. It is unclear regarding the specific chemical composition of the metabolite of milnacipran that is administered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 9, 11 – 13, 15 – 17, 19 – 21, 23, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Paillard *et al.* (WO 98/08495), whereby US 6,699,506 is relied upon for English translation.

Paillard discloses a pharmaceutical composition with prolonged release for oral administration of a single daily dose of 50 to 240 mg of milnacipran (column 1, line 30 – 35). The formulation meets the limitation of a pulsed-release formulation because between 10 – 55% of the dose is released in 2 hours, between 40 – 75% of the dose is released in 4 hours, between 70 – 90% of the dose is released in 8 hours, and between 80 – 100% of the dose is released in 12 hours. A racemic mixture or pure enantiomeric forms of milnacipran may be administered (column 1, line 65 – column 2, line 3). The formulation comprises a mixture of microparticles that release the drug at different times (see column 1, lines 30 – 53). The formulation may comprise gelatin or sucrose, which are within the scope of a nutritional agent recited in claim 9 of the instant application

(see column 4, lines 19 – 20). The microparticles or microgranules contain a coating such as Eudragit NE30D, RS 100, RL 100, etc... (column 6, lines 45 – 68). Because the same dosage ranges of milnacipran also comprise a coating, as claimed, the formulation would inherently have the same dosage release patterns, blood plasma concentrations, and thus a reduced intensity of milnacipran side effects. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of anticipation has been established. See, for example, *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). With regard to claim 21, the dosage patterns can be interpreted to represent dosage escalation, as drug dosages increase over time. Regarding claim 23, the method of production of the formulation is disclosed, and the formulation is "provided" (column 2, lines 9 - 14). With regard to claim 24, the milnacipran formulation is orally administered (abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 – 13, 15 – 17, 19 – 21, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paillard *et al.* in view of Watanabe *et al.* (US 7,008,640).

Paillard discloses a pharmaceutical composition with prolonged release for oral administration of a single daily dose of 50 to 240 mg of milnacipran (column 1, lines 30 – 35). The milnacipran is released in pulses, as different amounts are released over time. Because the same dosage ranges of milnacipran also comprise a coating, as claimed, the formulation would inherently have the same dosage release patterns, blood plasma concentrations, and reduced intensity of milnacipran side effects.

Paillard does not teach a milnacipran formulation in combination with another drug.

Watanabe teaches a pharmaceutical composition for oral use with improved absorption, which comprises a drug, aminoalkyl methacrylate copolymer E, and an acidic substance (abstract). Regarding claims 1, 9, and 10, the drug may be milnacipran (column 11, line 9), and may comprise a single drug or may be a mixture of two or more compounds (i.e. an analgesic, an anti-inflammatory agent, an antihistamine, etc., or acetaminophen, ibuprofen, etc.. (column 10-11)). The drug may include optical isomers or stereoisomers of the compound, and mixtures of these isomers (column 9, lines 47 – 58). The pharmaceutical composition may be a timed-release or pulsed-release pharmaceutical preparation and may be in microparticle form (column 16, lines 7 – 12). The pharmaceutical composition may be coated with an enteric substance (column 15, lines 10 – 13). A method for making the pharmaceutical composition is disclosed, and comprises the step of providing a formulation that meets the limitations of the instant claims (claim 2). Regarding claim 24, the pharmaceutical composition is administered to a patient in an effective amount and reduced adverse effects are expected (column 12, line 26 – 35).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the modified release milnacipran formulation taught by Paillard with the pharmaceutical composition taught by Watanabe which may be formulated as a pulsed-release composition, may comprise milnacipran, and may be administered in combination with another drug, and that the preparation and use of such formulations could be accomplished with a reasonable expectation of success. Both

references teach that the motivation for preparing and using these formulations is to minimize adverse side effects of the drug.

Claims 1 – 13, 15 – 21, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paillard *et al.* in view of Menza *et al. (J. Clin. Psychiatry*, 2000, 61(5), p. 378-81).

Paillard discloses a pharmaceutical composition with prolonged release for oral administration of a single daily dose of 50 to 240 mg of milnacipran (column 1, lines 30 – 35). The milnacipran is released in pulses, as different amounts are released over time. Because the same dosage ranges of milnacipran also comprise a coating, as claimed, the formulation would inherently have the same dosage release patterns, blood plasma concentrations, and reduced intensity of milnacipran side effects.

Paillard does not teach a milnacipran formulation in combination with modafinil.

Menza teaches doses of 100 to 200 mg a day of modafinil in combination with antidepressants for treatment of depression (abstract).

Menza does not teach modafinil in combination with milnacipran as the specific antidepressant.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the formulation of Paillard comprising milnacipran for the treatment of depression, with modafinil because both drugs (i.e. milnacipran and modafinil) have been used previously within the range of the claimed dosages in the treatment of depression. One would have expected to have a reasonable expectation

of success in doing so because Menza specifically teaches the motivation to utilize modafinil as an augmenter to antidepressants in the treatment of depression.

Claims 1 – 13, 15 – 17, 19 – 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paillard *et al* in view of Ansseau *et al.* (*Psychopharmacology*, 1994, 114, p. 131-137).

Paillard discloses a pharmaceutical composition with prolonged release for oral administration of a single daily dose of 50 to 240 mg of milnacipran (column 1, lines 30 – 35). The milnacipran is released in pulses, as different amounts are released over time. Because the same dosage ranges of milnacipran also comprise a coating, as claimed, the formulation would inherently have the same dosage release patterns, blood plasma concentrations, and reduced intensity of milnacipran side effects.

Paillard does not specify the administration of milnacipran at bedtime.

Ansseau teaches a once daily dosage of 100 mg of milnacipran for the treatment of depression that was administered in the evening (p. 136).

Ansseau does not teach a modified release formulation of milnacipran.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the formulation of Paillard with the method of administration of milnacipran in the evening (i.e. bedtime) as taught by Ansseau. One would have expected to have a reasonable expectation of success in doing so because Ansseau specifically teaches that a single evening administration of milnacipran in the evening is not as effective as twice daily administration, likely due to inadequate plasma levels

since the plasma elimination half-life of milnacipran is about 7 hours (p. 136), and the formulation of Paillard was known to provide prolonged dosages of the drug.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lhs

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER